**DETAILED ACTION**

1. Claims 1, 18, 29-33 and 37 are pending.

2. Claims 30, 32 and 33 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. Claims 1, 18, 29, 31 and 37 are being acted upon in this Office Action.

4. The enablement rejection of claims 1-2, 29 and 31 under 35 U.S.C. 112, first paragraph has been obviated by the claims amendment filed February 22, 2010.

5. The written description rejection of claims 1-2, 29 and 31 under 35 U.S.C. 112, first paragraph, has been obviated by the claims amendment filed February 22, 2010.

6. The rejection of claim under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been obviated by the claims amendment filed February 22, 2010.

7. A telephone call was made to Applicant's representative Thomas J Kowalski on May 20, 2010 that upon reconsideration, a further Office action will be issued.

New Ground of Rejection

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 18, 29 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. **This is New Matter**.

The recitation of antibody or binding fragment thereof which binds to an MHC class II molecule in claim 1 has no written support in the specification and the claims as originally filed.

The recitation of antibody or binding fragment which binds to an MHC class II molecule in claim 18 has no written support in the specification and the claims as originally filed.

The specification discloses the first sequence comprises a polypeptide which is capable of binding to another APC surface molecule. Such APC molecules include: CD205 (DEC205), CD204 (Scavenger receptor), CD14, CD206 (Mannose receptor), TLRs, Langerin (CD207), DC-SIGN (CD209), Fc), receptor 1 (CD64) and Fc), receptor 2 (CD32), CD68, CD83, CD33, CD54 and BDCA-2,3,4, see page 13, line 5-9.

It will be appreciated that the first sequence may therefore take the form of an antibody to an APC surface molecule. In a preferred embodiment the antibody is generated against the APC extracellular domain of the APC surface molecule, or a fragment thereof. The production of antibodies is described in for example Kohler and Milstein (1975) Nature 256:495-497, see page 13, lines 11-15.

The specification discloses superantigen as a first polypeptide that binds to MHC class II, see page 13, lines 1-3. As such, the specification does not describe *antibody* to MHC class II molecule, much less binding fragment thereof that bind to MHC class II molecule on the surface of antigen representing cell (APC).

With respect to claim 29, the specification does not adequately describe the polypeptide comprising the six CDRs of any antibody or binding fragment thereof that binds to MHC class II molecule, CD205 (DEC205), CD204 (Scavenger receptor), CD14, CD206 (Mannose receptor), TLRs, Langerin (CD207), DC-SIGN (CD209), Fc), CD68, CD83, CD33, CD54 and BDCA-2,3,4 in the claimed fusion protein. As such, it follows that the *polynucleotide* sequence encoding such antibody or binding fragment thereof fused to SEQ ID NO: 40, or SEQ ID NO: 42 or SEQ ID NO: 43 or SEQ ID NO: 44 is not adequately described.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 18, 29, 31 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 7,030,228 B1 (filed November 15, 2000; PTO 892) in view of US application 2005/0137130 A1 (filed May 14, 2004; PTO 892).

The '228 patent teaches fusion protein comprising an antibody such as anti-BDCA-2 or anti-BCDA-3 or anti-BDCA-4 or binding fragment thereof such as Fab and F(ab')2 as the first polypeptide that binds to an APC surface molecule such as BDCA-2 or BCDA-3 or BDCA-4, respectively, wherein the antibody or binding fragment thereof is fused to a second polypeptide or an effector molecule such as cytokine or toxin (see col. 16, lines 64-67, col. 17, Table 1, col. 19, lines 16 through col. 20, lines 1-13, col. 21, lines 11-32, in particular). The reference fusion protein is useful for targeting the drug of interest to antigen presenting cells (see col. 16, lines 51-56, in particular). The '228 patent teaches a composition comprising the reference fusion protein and pharmaceutical acceptable carrier (see col. 37, line 60 through col. 38, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the fusion protein wherein the second polypeptide is human Delta 1 comprising the amino acid sequence of SEQ ID NO: 40.

The US application 2005/0137130 teaches human Delta 1 comprising the amino acid sequence of SEQ ID NO: 51, which is 100% identical to the claimed SEQ ID NO: 40 (see reference SEQ ID NO: 51, Figure 4A, in particular). The publication further teaches human notch ligand fragment consisting of residues 159-221, which is 100% identical to the claimed fragment of SEQ ID NO: 25 (see Figure 5, DLL1Human/159-221, in particular). The advantage of using such soluble Notch ligand is that it provides effective inhibition of Notch signaling with

little or no competing agonist activity and such polypeptide may also be easier to produce in bacterial expression system (see paragraph 0094, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the cytokine or toxin in the fusion protein comprising antibody or binding fragment thereof that binds to BDCA-2, BDCA-3 or BCDA-4 of the '228 patent for the Delta 1 comprising the amino acid sequence of SEQ ID NO: 51 or fragment thereof as taught by the US application 2005/013710. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do substitute one known effector molecule for another known effector molecule because US application 2005/0137130 teaches human Delta 1 or fragment thereof is effective for inhibition of Notch signaling with little or no competing agonist activity and such polypeptide may also be easier to produce in bacterial expression system (see paragraph 0094, in particular).

One having ordinary skill in the art would have been motivated to fuse any one of the antibody such as anti-BDCA-2 or anti-BCDA-3 or anti-BDCA-4 or binding fragment thereof such as Fab, F(ab')2 to the human Delta 1 or fragment thereof because the antibody or binding fragment thereof in the fusion protein is useful for targeting the drug of interest to antigen presenting cells by binding to BDCA expressed on antigen presenting cells thereby eliminating some of the toxicity and less dose is needed as a pharmaceutical composition (see col. 16, lines 51-56, in particular). Claim 29 is included in this rejection because the reference fusion protein is made recombinantly by transforming host cell such as *E coli* with an expression vector such as pET-22b comprising a polynucleotide encoding the fusion protein as taught by the '228 patent (see col. 24, line 33 through 56, in particular).

Given the examination guidelines for determining obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in *KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007)* and the Examination Guidelines set forth in the Federal Register (Vol. 72, No. 195, October 10, 2007) and incorporated recently into the MPEP (Revision 6, September 2007), the following rationales to support rejection under 35 U.S.C. 103(a) are noted:

A) Combining prior art elements according known methods to yield predictable results.
B) Simple substitution of one known element for another to obtain predictable results.

C) Use of known technique to improve similar products in the same way.

D) Applying known technique to a known product ready for improvement to yield predictable results.

E) "Obvious to try" --- choosing form a finite number of identified, predictable solutions, with a reasonable expectation of success.

F) Some teachings, suggestion, or motivation in the prior art that would lead to one of ordinary skill to modify the prior art reference to arrive at the claimed invention.

In this case, combining prior art elements according known method would yield predictable results. Simple substitution of one known element cytokine or toxin in fusion protein for another effector molecule human Delta 1 would obtain predictable results.

Obviousness is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007).* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The IFW official Fax number is (571) 273-8300.

15. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
May 21, 2010